



Complete Summary

GUIDELINE TITLE

ACR Appropriateness Criteria® follow-up of malignant or aggressive musculoskeletal tumors.

BIBLIOGRAPHIC SOURCE(S)

Roberts CC, Daffner RH, Weissman BN, Bennett DL, Blebea JS, Jacobson JA, Morrison WB, Resnik CS, Rubin DA, Schweitzer ME, Seeger LL, Taljanovic M, Wise JN, Payne WK, Expert Panel on Musculoskeletal Imaging. ACR Appropriateness Criteria® follow-up of malignant or aggressive musculoskeletal tumors. [online publication]. Reston (VA): American College of Radiology (ACR); 2008. 12 p. [54 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Manaster BJ, Petersen B, Dalinka MK, Rubin DA, Rosen G, Lackman R, Janjan N, Expert Panel on Musculoskeletal Imaging. Follow-up of malignant or aggressive musculoskeletal tumors. [online publication]. Reston (VA): American College of Radiology (ACR); 2006. 11 p. [46 references]

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT
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SCOPE

DISEASE/CONDITION(S)

- Musculoskeletal tumors
- Metastatic disease

GUIDELINE CATEGORY

Diagnosis
Evaluation

CLINICAL SPECIALTY

Internal Medicine
Nuclear Medicine
Oncology
Radiology

INTENDED USERS

Health Plans
Hospitals
Managed Care Organizations
Physicians
Utilization Management

GUIDELINE OBJECTIVE(S)

To evaluate the appropriateness of follow-up radiologic examinations for patients with malignant or aggressive musculoskeletal tumors

TARGET POPULATION

Patients with malignant or aggressive musculoskeletal tumors

Note: These guidelines are not intended for use in the following patients:

- Patients with metastatic disease from other primaries
- Patients with head and neck tumors
- Patients with spine tumors
- Patients with chest wall tumors
- Patients with multiple myeloma
- Patients with benign or nonaggressive bone or soft-tissue tumors
- Patients evaluated for chemotherapy or radiation therapy effectiveness, preoperatively after such induction therapy

INTERVENTIONS AND PRACTICES CONSIDERED

1. Timing, frequency, and duration of follow-up examinations
2. Computed tomography (CT), area of interest, without contrast
3. Fluorodeoxyglucose-positron emission tomography (FDG-PET), whole body
4. X-ray, area of interest
5. Nuclear medicine (NUC), technetium (Tc)-99m bone scan, whole body
6. Magnetic resonance imaging (MRI), area of interest, with or without contrast

7. Ultrasound (US), alone or with color Doppler flow imaging

MAJOR OUTCOMES CONSIDERED

Utility of radiologic examinations in differential diagnosis

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches of peer-reviewed medical journals, and the major applicable articles were identified and collected.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

One or two topic leaders within a panel assume the responsibility of developing an evidence table for each clinical condition, based on analysis of the current literature. These tables serve as a basis for developing a narrative specific to each clinical condition.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Since data available from existing scientific studies are usually insufficient for meta-analysis, broad-based consensus techniques are needed to reach agreement in the formulation of the appropriateness criteria. The American College of Radiology (ACR) Appropriateness Criteria panels use a modified Delphi technique to arrive at consensus. Serial surveys are conducted by distributing questionnaires to consolidate expert opinions within each panel. These questionnaires are distributed to the participants along with the evidence table and narrative as developed by the topic leader(s). Questionnaires are completed by the participants in their own professional setting without influence of the other members. Voting is conducted using a scoring system from 1-9, indicating the least to the most appropriate imaging examination or therapeutic procedure. The survey results are collected, tabulated in anonymous fashion, and redistributed after each round. A maximum of three rounds is conducted and opinions are unified to the highest degree possible. Eighty percent agreement is considered a consensus. This modified Delphi technique enables individual, unbiased expression, is economical, easy to understand, and relatively simple to conduct.

If consensus cannot be reached by the Delphi technique, the panel is convened and group consensus techniques are utilized. The strengths and weaknesses of each test or procedure are discussed and consensus reached whenever possible. If "No consensus" appears in the rating column, reasons for this decision are added to the comment sections.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

It is generally accepted that computed tomography (CT) is more accurate in diagnosing lung parenchymal metastatic disease than is chest radiography. However, that increased accuracy may not translate to a positive cost-benefit analysis. One excellent review article quotes a retrospective study of 125 consecutive patients in which, for low-risk patients (primary tumor <5 cm), the incremental cost effectiveness ratio was \$59,722 per case of synchronous pulmonary metastases when chest CT was added to chest radiography. This suggested to the authors that the yield for an added CT scan is low when a good quality chest radiograph does not reveal any suspicion for lung metastases. Based on this, the authors recommend surveillance for lung metastases in the low-risk patient (primary tumor <5 cm) by chest radiograph alone. In the high-risk category (primary tumor >5 cm), this study found that initial staging chest CT was cost effective, but recommended follow-up only by chest radiography. However, given the higher accuracy of CT, as well as the fact that pulmonary metastases from sarcomas are frequently cured by surgical excision, it is likely that the use of CT for staging and surveillance for lung metastases will continue.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

ACR Appropriateness Criteria®

Preface to the Tables of Variants

Musculoskeletal tumor follow-up requires decisions regarding imaging method and timing, when assessing for local recurrence and metastatic disease.

- Variants 1 and 2 address modality and timing of follow-up for metastatic disease to the lung from a musculoskeletal primary (low and high grade, respectively).
- Variant 3 addresses the modality and timing of follow-up for osseous metastatic disease from a musculoskeletal primary.
- Variant 4 addresses the timing of follow-up for local recurrence.
- Variants 5, 6, and 7 address the modality for follow-up in osseous tumors without hardware, osseous tumors with hardware, and soft-tissue tumors, respectively.

Clinical Condition: Follow-up of Malignant or Aggressive Musculoskeletal Tumors

Variant 1: Lower risk patient (low grade). Evaluation for metastatic disease to the lung from musculoskeletal primary.

Radiologic Procedure	Rating	Comments	RRL*
Modality for Baseline Examination			
CT chest without contrast	9	Despite some of the cost analysis studies, the panel believes early diagnosis of lung metastases is critical and that chest CT should be performed. If chest CT is done, chest x-ray is not necessary.	Med
FDG-PET whole body	5	In individual cases, can be a good problem solving tool. Outcomes data on PET/CT are pending. The CT portion of PET/CT, although unenhanced, can include thin section images through the whole body, which can enhance diagnosis.	High
X-ray chest	3		Min

Radiologic Procedure	Rating	Comments	RRL*
Modality for Follow-Up Examination			
CT chest without contrast	9		Med
FDG-PET whole body	4	Can be a useful problem solving tool if another study is equivocal.	High
X-ray chest	3		Min
Timing of First Postoperative Examination			
3-6 months postoperative	9		NS
Frequency of Follow-Up			
Every 3-6 months	9		NS
Every 6-12 months	2		NS
Duration of Follow-Up			
10 years	9	After 5 years, frequency can decrease to every 6-12 months.	NS
5 years	2		NS
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: Higher-risk patient (high grade). Evaluation for metastatic disease to the lung from musculoskeletal primary.

Radiologic Procedure	Rating	Comments	RRL*
Modality for Baseline Examination			
CT chest without contrast	9	Despite some of the cost analysis studies, the panel believes early diagnosis of lung metastases is critical and that chest CT should be performed. If chest CT is done, chest x-ray is not necessary.	Med
FDG-PET whole	7	In individual cases, can be a good	High

Radiologic Procedure	Rating	Comments	RRL*
body		problem-solving tool. PET/CT appears to be emerging as a primary diagnostic tool as well for diagnosing metastatic disease in many musculoskeletal tumors.	
X-ray chest	2		Min
Modality for Follow-Up Examination			
CT chest without contrast	9		Med
FDG-PET whole body	5	Can be a useful problem-solving tool if another study is equivocal.	High
X-ray chest	2		Min
Timing of First Postoperative Examination			
3-6 months postoperative	9		NS
Frequency of Follow-Up			
Every 3-6 months	9		NS
Every 6-12 months	2		NS
Duration of Follow-Up			
10 years	9	After 5 years, frequency can decrease to every 6-12 months.	NS
5 years	2		NS
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 3: Evaluation for osseous metastatic disease from musculoskeletal primary.

Radiologic Procedure	Rating	Comments	RRL*
Timing of Baseline Examination			

Radiologic Procedure	Rating	Comments	RRL*
Only if symptomatic	9	Although additional imaging should be provided only if the patient is symptomatic, it should be noted that in many cases, baseline whole body PET/CT would already have been done for lung, which provides high sensitivity for some bone tumors.	NS
Frequency of Follow-Up			
Only if symptomatic	9		NS
Duration of Follow-Up			
Only if symptomatic	9		NS
Modality for Follow-up Examination			
FDG-PET whole body	7	In individual cases, can be a good problem solving tool. Sclerotic lesions are more difficult to detect with PET but are well demonstrated on the CT portion of the PET/CT exam.	High
NUC TC-99m bone scan whole body	5		Med
MRI whole body without contrast	3	Problem solving tool or staging for second surgery.	None
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 4: Surveillance for local recurrence.

Radiologic Procedure	Rating	Comments	RRL*
Timing of Baseline Exams			
3-6 months postoperative	9		NS
Frequency of Follow-Up			

Radiologic Procedure	Rating	Comments	RRL*
At 3 months or before 6 months	9		NS
At 6 months or before 9 months	2		NS
At 9 months or before 12 months	2		NS
Duration of Follow-Up			
10 years	9	After 5 years, frequency can decrease to every 12 months or be performed earlier if symptomatic	NS
3 years	1		NS
5 years	2		NS
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 5: Osseous tumor, without significant hardware present. Local recurrence.

Radiologic Procedure	Rating	Comments	RRL*
X-ray area of interest	9	Both MRI and x-ray are indicated.	NS
MRI area of interest with or without contrast	9	Both MRI and x-ray are indicated. Contrast administration helpful for further evaluation of equivocal findings. See comments regarding contrast in the text below under "Anticipated Exceptions."	None
FDG-PET whole body	4	Can be a useful problem-solving tool if another study is equivocal.	High
CT area of interest without contrast	4	On a case-by-case basis, CT may be useful. Useful in osseous tumor when better definition of bony anatomy is needed.	NS

Radiologic Procedure	Rating	Comments	RRL*
US area of interest	1		None
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 6: Osseous tumor, with significant hardware present. Local recurrence.

Radiologic Procedure	Rating	Comments	RRL*
X-ray area of interest	9		NS
MRI area of interest with or without contrast	7	Can use metal suppression techniques. Contrast administration helpful for further evaluation of equivocal findings. Since fat suppression is inhomogeneous with adjacent hardware, pre- and post-contrast subtraction postprocessing is recommended. See comments regarding contrast in the text below under "Anticipated Exceptions."	None
FDG-PET whole body	5	Can be a useful problem-solving tool if another study is equivocal.	High
CT area of interest without contrast	5	Can be useful if MRI not informative. Alter technique to decrease metal artifact.	NS
US area of interest	2		None
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 7: Soft-tissue tumors; presume no significant hardware. Local recurrence.

Radiologic Procedure	Rating	Comments	RRL*
MRI area of interest with or without contrast	9	Contrast administration helpful for further evaluation of equivocal findings. See comments regarding contrast in the text below under "Anticipated Exceptions."	None
FDG-PET whole body	6	Can be a useful problem-solving tool if another study is equivocal. Outcomes data on PET/CT are pending. The CT portion of PET/CT includes thin-section images through the whole body, which can enhance diagnosis.	High
X-ray area of interest	2	Problem solver if needed to interpret findings on MRI	NS
CT area of interest without contrast	2	Postoperative scarring can obscure local recurrence.	NS
US area of interest	2		None
<u>Rating Scale: 1=Least appropriate, 9=Most appropriate</u>			*Relative Radiation Level

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

This topic specifically excludes: 1) metastatic disease from other primaries; 2) head and neck tumors; 3) spine tumors; 4) chest wall tumors; 5) multiple myeloma; 6) benign or nonaggressive bone or soft-tissue tumors; and 7) evaluation for chemotherapy or radiation therapy effectiveness, preoperatively after such induction therapy.

It should be noted that there is a lack of controlled studies in the literature that directly address the issue of tumor follow-up, and the recommendations are based mostly on consensus, are subject to changes later if new data come out, and should be used only as a guideline with generous opportunity for modification in individual circumstances.

This topic addresses two issues of follow-up for tumor therapy: the timing of the follow-up examination, and the type of imaging best used for follow-up.

Ideally, the timing of follow-up for tumor recurrence or metastatic disease would be individualized for each tumor type and each patient. To design a follow-up protocol, one would generally wish to know the following: 1) How good is the

imaging test to be used for detecting the presence of tumor? 2) How important is early detection of relapse, related to salvage effectiveness (utility/risk analysis)? and 3) When is the relapse most likely to occur (hazard rate)? Individual hazard rate is related to tumor type, grade, size, and central location; patient age and gender; tumor stage; type of treatment; and surgical margins. Overall, the goal of an imaging protocol is to concentrate testing when the relapse is most likely to occur. This presumes that testing frequency should gradually decrease over time. There are outstanding reviews of model development for such protocols in lymphoma and other tumors. However, such models do not exist for extremity tumors.

Because models relating to the hazard rate and utility/risk analysis do not exist for individual extremity tumor types, the guideline developers will consider the sarcomas as a group and try to evaluate general local recurrence rate and timing as well as metastatic rate and timing. The most helpful general information can be found in several articles. The information most commonly agreed to among these authors is that approximately 80% of patients who recur locally or systemically will do so within 2 years of their primary treatment. This suggests that the most aggressive follow-up should occur in the first 2 years, with tapering of imaging after that time.

Timing and Frequency of Follow-Up

The incidence of metastatic disease varied considerably in the large studies mentioned above. The incidence of metastatic disease only to the lung ranged from 18%-52%. In another study, 31% of patients had metastatic disease, of whom 42% previously had a local recurrence. In at least some of these studies, it appears as though the incidence of local recurrence is less frequent than the occurrence of metastatic disease in high-grade sarcomas. Therefore, local failure may not be the initiating factor in most systemic metastases. This finding suggests that follow-up studies should include systemic surveillance as well as imaging for local recurrence.

Of the systemic metastases, lung metastasis is by far the most frequent. It is generally accepted that computed tomography (CT) is more accurate in diagnosing lung parenchymal metastatic disease than is chest radiography. However, that increased accuracy may not translate to a positive cost-benefit analysis. One excellent review article quotes a retrospective study of 125 consecutive patients in which, for low-risk patients (primary tumor <5 cm), the incremental cost effectiveness ratio was \$59,722 per case of synchronous pulmonary metastases when chest CT was added to chest radiography. This suggested to the authors that the yield for an added CT scan is low when a good quality chest radiograph does not reveal any suspicion for lung metastases. Based on this, the authors recommend surveillance for lung metastases in the low-risk patient (primary tumor <5 cm) by chest radiography alone. In the high-risk category (primary tumor >5 cm), this study found that initial staging chest CT was cost effective, but recommended follow-up only by chest radiography. However, given the higher accuracy of CT, as well as the fact that pulmonary metastases from sarcomas are frequently cured by surgical excision, it is likely that the use of CT for staging and surveillance for lung metastases will continue.

In terms of frequency of follow-up, some experts recommend that high-risk patients be followed with chest radiography every 3 months for 2 years, every 4 months for the next 2 years, every 6 months for the 5th year, and annually after that. The recommendation from another review based on the experiences of two large tumor centers for low-risk patients is similar, calling for chest radiograph for pulmonary metastatic surveillance every 3-4 months for 2 years, every 4-6 months for the next 2 years and yearly after that. Six-month imaging is widely regarded by other experts as a suitable compromise between intense surveillance and early lesion detection. The optimal frequency and modality of follow-up imaging have not been scientifically established.

The frequency of other distant metastatic disease ranges from 14%-20%. It is debatable whether surveillance for osseous metastases or lymphatic metastatic disease is cost-efficient. If required, technetium bone scan is most frequently used; with care, whole body magnetic resonance imaging (MRI) can detect osseous metastases with reasonable sensitivity and specificity. Opposed phase gradient echo sequences may be used to improve specificity when equivocal marrow changes are seen on MRI.

The use of 2-(fluorine-18)fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) has been shown to be effective in localizing metastases from many bone sarcomas, though it may be nonspecific and produces false negatives in osteosarcoma bone metastases. Although bone scan, FDG-PET, and MRI may detect osseous metastases, these studies are generally not advocated as part of the initial workup or follow-up for osseous metastases in asymptomatic cases.

Metastatic disease from primary extremity liposarcoma deserves special note. A study retrospectively looking at 122 patients with extremity liposarcoma found that the myxoid type (86% of liposarcomas in this series) tended to metastasize to extrapulmonary sites, frequently involving the trunk or retroperitoneum. A biopsy proven "primary" myxoid liposarcoma in the trunk or retroperitoneum should prompt a rigorous search for an occult extremity primary.

Local recurrence can be as low as 10%-20% using multimodality therapy as well as limb-sparing surgery and may be routinely as low as 10% in patients with high-grade sarcomas smaller than 5 cm at the time of diagnosis. Local recurrence ranged from 20%-52% in the two largest studies. Different studies have related local failure to tumor grade and size as well as to type of resection. A multivariate analysis of 15 factors demonstrated marginal excision, tumor necrosis, and extracompartmental location to be the greatest factors relating to local recurrence, but the greatest factors relating to survival include local recurrence, high grade, male gender, and extensive necrosis. One study found that local recurrence does not correlate with tumor size, although metastatic disease does. Similarly, local recurrence does not correlate with location proximal to the original tumor or grade, but the likelihood of metastatic disease does. Local recurrence in this study related most strongly to the "quality" of local treatment. In another study, long-term survival was influenced only by positive surgical margins. Another study noted specifically that, compared with ablative surgical procedure, limb-sparing surgery itself has a 3- to 5-fold increased risk of local relapse, which significantly worsens the prognosis.

Because of the different findings, it would seem reasonable to establish a routinely suggested timing sequence for evaluating local recurrence, with the caveat that for marginal excision, in the presence of large regions of necrosis and high-grade or site evaluation, more frequent follow-up may be efficacious. One retrospective analysis drawing on a review of 1,500 patients from Memorial Sloan-Kettering Cancer Center and the M.D. Anderson Cancer Center, recommended follow-up of adult soft tissue sarcomas based on low and high risk of recurrence. Risk stratification was based on size of primary neoplasm (T1: low risk <5cm; T2: high risk >5cm). For local recurrence in low-risk patients the recommendation was for "cross-sectional imaging of choice" individualized for patient and location of primary tumor. The implication is that for extremity primaries the clinical examination may obviate the need for routine cross-sectional imaging follow-up in the low-risk group. Cross-sectional imaging follow-up for less accessible areas (trunk or retroperitoneum) would be required at 3-4 month intervals for 2 years, 4-6 month intervals for 2 years, and yearly thereafter. Within the low-risk group, surveillance could stop after 5-10 years.

Within the high-risk group local recurrence rate was noticeably higher, and the analysis recommended cross-sectional imaging every 3 months for 2 years, every 4 months for the next 2 years, every 6 months for the 5th year, and then annually. A study looking at long-term follow-up (greater than 5 years) of patients with primary extremity sarcoma showed that 21% of patients alive at 5 years will die of their disease in the next 5 years. In a multifactorial analysis, a positive surgical margin was the only factor that showed positive predictive value for long-term recurrence. Size, grade, age, and depth were not shown to increase long-term recurrence, and local recurrence did not correlate to increased mortality after 5 years. These data may necessitate a more tailored approach to follow-up of patients with bone or soft-tissue sarcoma. Patients with T2 primaries need to be followed more closely than those with T1 primaries, and those with positive surgical margins may need longer surveillance than those with complete excision.

Implications of Tumor Type and Therapy

The specific type of imaging for follow-up for local recurrence will depend on the site of the original tumor (osseous vs. soft tissue), as well as the type of therapy used (curettage with bone graft vs. resection with allograft vs. soft-tissue resection, all taking into account the presence or absence of hardware). The following comments relate to each of these situations.

One reference suggests that patients treated with curettage and bone chip allografts can be followed by MRI. It suggests that most cases will have a speckled bright signal on T2 imaging and that, if signal intensity on both T1 and T2 imaging is predominantly low, there is a reasonable likelihood that this does not represent recurrence. One study discusses the MRI follow-up of patients with curettage and bone grafting plus cryosurgery. Many of these cases showed a zone beyond the surgical margins that is low signal on T1 and high signal on T2, the thickness of which ranges from 1 to 17 mm, varying within a single patient.

The evaluation of large allografts used in treating sarcomas is discussed in several articles. Most of these studies used only radiographs. They indicate that there is a high complication rate (40%-57%). The complications include infection (6%-25%), usually occurring in the first 12 months; the patient may present with a

mass. Fracture is a common complication as well, ranging from 15%-27% and occurring in the first 3 years. Tumor recurrence in these series ranged from 0%-16% and generally occurred in 12-24 months. After 4 years, there is late development of articular degeneration if the graft is an osteoarticular type. Technetium bone scanning may reflect the physiology of allograft incorporation, but it has not been advocated to detect local recurrence. Also, specific CT appearance is described, showing initial thinning of the cortex and very prominent subcortical cyst formation as well as a differential in attenuation between the graft and host bone. One extremely small study of MRI of allografts showed a very heterogeneous T1 and T2 signal but was inadequate in scope for further information to be derived. It seems that radiographs are usually used for follow-up of massive allografts because of the large amount of hardware that is generally present. However, the authors note that multislice CT with reformatting in coronal or sagittal planes can minimize metallic artifact and can be extremely useful in evaluating for either union or allograft to host bone or for osseous complications. Most of the complications relate to failure of the graft or infection.

Recurrence involving only the soft tissues could be detected by ultrasound (US) if too much hardware is present to evaluate with other imaging. PET has emerged as a powerful tool for evaluating local recurrence in the face of suboptimal cross-sectional imaging because of large amounts of metal. PET and its possible applications are addressed separately below.

Magnetic Resonance Imaging, Computed Tomography, and Ultrasound

Two studies evaluated MRI of both soft tissue and bone tumors in follow-up. Both emphasize that high signal intensity on T2 can be seen for a number of non-neoplastic reasons. These include presence of a postoperative seroma, hematoma, changes related to radiation therapy, fat necrosis, packing material, allograft, scar tissue, and bowel or bladder herniation. Although the timing of the study and knowledge of details of the case can be very valuable in sorting out these possibilities, in some cases they did not obviate biopsy. The larger of the studies, with 60 patients in follow-up, showed that if there is a lesion that is of low signal intensity on T2, it generally does not represent recurrent tumor (sensitivity 96%). If there is a lesion with high signal intensity on T2 and surgery was the only therapy used, tumor recurrence is a high likelihood. If radiation therapy as well as surgery has been used, high signal intensity is nonspecific for distinguishing between radiation-induced inflammation and recurrent tumor. In that study, 66% of patients had high signal intensity on T2, and the overall sensitivity for detection of tumor recurrence was only 70%.

In evaluating whether CT or MRI is more efficacious in follow-up of sarcomas, one should discount the Radiology Diagnostic Oncology Group (RDOG) report in which no statistical difference was found between CT and MRI in determining tumor involvement of bone, muscle, joints, or neurovascular structures because this study did not address questions of follow-up. However, one study demonstrates that CT does not differentiate between tumor recurrence and scar, since both enhance.

Few studies advocate the use of US in follow-up for soft-tissue masses. A study performed in 1991 compared MRI and US in follow-up of soft-tissue sarcoma. The sensitivity and specificity of MRI for local recurrence were 83% and 93%,

respectively, while those for US were 100% and 79%, respectively. These differences were not statistically significant. It is noted that acute postoperative changes make US diagnosis difficult (particularly in the first 3-6 months postoperatively). Note was also made that US may be particularly helpful in detecting recurrences that have short T2 relaxation times. This particular article recommends baseline US and MRI, followed by US. If subsequent US scans are inconclusive, MRI with contrast is recommended. The findings of these and other articles are difficult to apply, as MRI has dramatically improved over the years since the studies were performed. Another article is biased, without cross-sectional imaging comparison but with favorable statistics on a prospective study of 50 consecutive patients with clinical suspicion of local recurrence. Twenty-four of 26 patients were confirmed as having recurrence, and 22 of 22 were accurately classified as no recurrence or benign masses (abscesses or lipoma) based on US examination. Discrete, hypoechoic, well-defined lesions were labeled as recurrence. Although these studies did not include osseous sarcoma follow-up, US in the presence of extensive hardware may be useful for follow-up for soft tissue mass in that situation. Color Doppler flow imaging may also help differentiate recurrent tumor mass from fibrous tissue or other nonvascular tissue in the postoperative tumor site; this may be particularly helpful in the presence of hardware and if there is a baseline postoperative Doppler study. These problem-solving utilities of US are useful in the absence of FDG-PET.

Several MRI studies have refined the methodology for evaluation and for recurrence of soft-tissue sarcomas. On the basis of a large number of examinations (511 examinations, 182 patients), one study showed that of the 102 examinations showing no high signal intensity mass, 101 had no recurrence. Seventy-nine of the patients had a high signal intensity on T2 but no mass; of these, only two had a local recurrence. Seventy-eight patients had high signal intensity on T2 with the presence of a mass. Sixty of these were proven to have recurrence, 24 had a seroma, and four had a radiation-induced pseudomass. Further evaluation with contrast showed that seromas do not enhance, whereas recurrences and radiation changes do enhance. A caveat here is that if there is a large area of necrosis, then tumor may not enhance. It was also noted that generally (with some areas of overlap), recurrences enhance earlier in a dynamic study than does radiation-induced pseudomass. Another report suggested that in regions of high signal intensity on T2-weighted imaging, T1-weighted images should be reviewed for normal "texture" of muscle to help differentiate recurrence from other etiologies of high signal intensity.

Very few follow-up protocols have been advocated. However, one study suggests an algorithm for following soft-tissue tumors postoperatively. This algorithm starts with T2 imaging. If a mass is present on T2-weighted imaging, it should be followed by T1-weighted sequences with and without contrast. This procedure generally distinguishes hematoma and seroma from tumor or inflammation. If necessary, this can be followed by dynamic enhanced imaging with subtraction postprocessing, which further helps differentiate tumors from inflammation. In this algorithm, if a region of high signal intensity is seen on T2-weighted imaging but there is no mass present, further evaluation with contrast imaging is not recommended. Reasonably enough, it is stated that there will be some exceptions to the above recommendations. This algorithm is supported by a recent article reporting 98 patients with seven local recurrences and three inflammatory pseudotumors. All but one recurrence was detected by T2-weighted imaging,

indicating that it is a logical way to start the examination. Although enhanced MRI with subtraction postprocessing characterizes recurrences better than routine sequences in most patients, it is advocated only if contrast injection is required for diagnosis. Based on these authors' experience, they advocate delaying the postoperative baseline scan for at least 6-8 weeks to allow postoperative changes subside; they acknowledge that 3- or 6-month follow-up MRI examinations may be too costly but reiterate that close follow-up is mandatory, especially if the surgical resection was intralesional or marginal.

FDG-PET and PET/CT

There has been a significant amount of literature exploring the utility of FDG-PET in evaluating recurrent soft-tissue and osseous sarcoma. The literature seems to support using FDG-PET in three scenarios: 1) as a problem-solving tool in equivocal cases of local recurrence detected by MRI in patients who have undergone limb salvage surgery and have postoperative and/or radiation change confounding accurate MRI assessment, 2) as a primary evaluation for local recurrence in patients with overwhelming metallic artifact precluding accurate assessment with MRI, and 3) as a confirmatory tool in equivocal cases of distant metastases.

First, FDG-PET has been shown to have a high sensitivity and specificity for local recurrence in those patients in whom postoperative change or significant hardware cause equivocal or nondiagnostic MR findings. For evaluating local recurrence FDG-PET sensitivity ranges from 88%-100% and specificity ranges from 92%-100%. Specifically in nine patients with equivocal or technically inadequate MRI, sensitivity and specificity were 100% for recurrence using FDG-PET scanning. Situations in which PET was falsely negative were in tumors of low histologic grade (two low-grade liposarcomas and one low-grade chondrosarcoma), and one false positive was caused by inflammation. Postradiation or postoperative inflammation did not seem to cause diagnostic difficulty due to significant differences in specific uptake values (SUV) between benign and malignant causes. Mean SUV of malignant recurrence ranged from 3.0-5.0, and benign etiologies ranged from <1-1.35.

Evaluation of distant metastases with FDG-PET has been compared to technetium bone scanning for osseous metastases and osseous recurrence, and to CT for lung metastases. For Ewing's sarcoma bony metastases (n=49) FDG-PET showed a sensitivity and specificity of 100% and 96%, respectively, compared to 71% and 92% for technetium bone scan. Interestingly FDG-PET was falsely negative in all 6 osteosarcoma bony metastases. This was in contrast to evaluation of recurrent osteosarcoma which showed PET to be effective (n=6) in correctly identifying these lesions. FDG-PET failed to equal CT in sensitivity for pulmonary metastases, but there were no PET positive lesions that were CT negative, implying that FDG-PET could be used to confirm lesions suspicious by CT.

It should be noted that all the literature cited above is for PET and not combined PET/CT. Virtually all clinical studies done today are PET/CT, which is reasonably expected to be a more powerful tool than either PET or CT alone, at least for selected musculoskeletal tumors. PET/CT may eventually rival MRI for local and distant tumor surveillance due to the increased information obtained from thin-slice CT through the entire body. Potential limitations of the CT portion of a

PET/CT study include lack of intravenous (IV) contrast and lack of breath-hold technique. Bone lesions identified on PET are not always visible on CT. Although PET/CT has a high positive predictive value when findings are concordant, the positive predictive value has been shown to markedly decrease when findings are discordant. Additional outcomes data for PET/CT are expected in the future as a result of the National Oncologic PET Registry (www.cancerpetregistry.org).

In summary, FDG-PET is an area of robust growth and research, with current evidence supporting its use as a problem-solving tool in equivocal cases of local or distant recurrence detected on MRI or CT. In addition it may have high utility in evaluating tumor recurrence in patients with orthopedic hardware that precludes accurate use of MRI or CT. Low sensitivity for low-grade neoplasms and insensitivity for bony metastases of osteosarcoma are exceptions that need to be considered by the interpreting and ordering physician. Routine use of PET/CT beyond a problem-solving role has not been widely advocated in the literature, though anecdotal experiences are increasing rapidly. The panel feels that this emerging technology deserves recognition as a problem-solving tool and as a primary diagnostic tool for metastatic lesion detection and surveillance, at least in high-grade musculoskeletal tumors. Furthermore, the results of current studies and recent experience warrant a systematic prospective multi-center evaluation of its clinical value in diagnosis, staging, response to therapy, and detecting recurrence and metastatic disease of bone and soft-tissue sarcomas. Any such study must include its influence on outcome as well as a cost-benefit analysis. The same might be said for much of the other imaging recommended in this document. The desired evidence-based data are difficult to obtain for bone and soft-tissue sarcomas. The guideline developers therefore strive for a logical consensus that allows for optimizing patient and cost benefit. The result must allow for some nonuniformity since clinical judgment remains of paramount importance in these cases.

Anticipated Exceptions

Nephrogenic systemic fibrosis (NSF, also known as nephrogenic fibrosing dermopathy) was first identified in 1997 and has recently generated substantial concern among radiologists, referring doctors and lay people. Until the last few years, gadolinium-based MR contrast agents were widely believed to be almost universally well tolerated, extremely safe and non-nephrotoxic, even when used in patients with impaired renal function. All available experience suggests that these agents remain generally very safe, but recently some patients with renal failure who have been exposed to gadolinium contrast agents (the percentage is unclear) have developed NSF, a syndrome that can be fatal. Further studies are necessary to determine what the exact relationships are between gadolinium-containing contrast agents, their specific components and stoichiometry, patient renal function and NSF. Current theory links the development of NSF to the administration of relatively high doses (e.g., >0.2mM/kg) and to agents in which the gadolinium is least strongly chelated. The U.S. Food and Drug Administration (FDA) has recently issued a "black box" warning concerning these contrast agents (http://www.fda.gov/cder/drug/InfoSheets/HCP/gcca_200705HCP.pdf).

This warning recommends that, until further information is available, gadolinium contrast agents should not be administered to patients with either acute or significant chronic kidney disease (estimated glomerular filtration rate [GFR] <30

mL/min/1.73m²), recent liver or kidney transplant or hepato-renal syndrome, unless a risk-benefit assessment suggests that the benefit of administration in the particular patient clearly outweighs the potential risk(s).

Abbreviations

- CT, computed tomography
- FDG-PET, fluorodeoxyglucose--positron-emission tomography
- Med, medium
- Min, minimal
- MRI, magnetic resonance imaging
- NS, not specified
- NUC, nuclear medicine
- Tc, technetium
- US, ultrasound

Relative Radiation Level	Effective Dose Estimated Range
None	0
Minimal	<0.1 mSv
Low	0.1-1 mSv
Medium	1-10 mSv
High	10-100 mSv
*RRL assignments are not included for some examinations. The RRL assignments for the IP (in progress) exams will be available in future releases.	

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on analysis of the current literature and expert panel consensus.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate selection and timing of radiologic imaging procedures for follow-up of patients with malignant or aggressive musculoskeletal tumors

POTENTIAL HARMS

- Fluorodeoxyglucose-positron emission tomography (FDG-PET) may produce false negative and false positive results.
- Some patients with renal failure who have been exposed to gadolinium contrast agents (the percentage is unclear) have developed nephrogenic systemic fibrosis (NSF), a syndrome that can be fatal. The U.S. Food and Drug Administration (FDA) has recently issued a "black box" warning concerning these contrast agents. This warning recommends that, until further information is available, gadolinium contrast agents should not be administered to patients with either acute or significant chronic kidney disease (estimated glomerular filtration rate [GFR] <30 mL/min/1.73m²), recent liver or kidney transplant or hepato-renal syndrome, unless a risk-benefit assessment suggests that the benefit of administration in the particular patient clearly outweighs the potential risk(s).

Relative Radiation Level (RRL)

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Additional information regarding radiation dose assessment for imaging examinations can be found in the American College of Radiology (ACR) Appropriateness Criteria® Radiation Dose Assessment Introduction document (see "Availability of Companion Documents" field).

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- An American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those exams generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring

- physician and radiologist in light of all the circumstances presented in an individual examination.
- It should be noted that there is a lack of controlled studies in the literature that directly address the issue of tumor follow-up, and the recommendations are based mostly on consensus, are subject to changes later if new data comes out, and should be used only as a guideline with generous opportunity for modification in individual circumstances.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Personal Digital Assistant (PDA) Downloads

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Roberts CC, Daffner RH, Weissman BN, Bennett DL, Blebea JS, Jacobson JA, Morrison WB, Resnik CS, Rubin DA, Schweitzer ME, Seeger LL, Taljanovic M, Wise JN, Payne WK, Expert Panel on Musculoskeletal Imaging. ACR Appropriateness Criteria® follow-up of malignant or aggressive musculoskeletal tumors. [online publication]. Reston (VA): American College of Radiology (ACR); 2008. 12 p. [54 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1998 (revised 2008)

GUIDELINE DEVELOPER(S)

American College of Radiology - Medical Specialty Society

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GUIDELINE COMMITTEE

Committee on Appropriateness Criteria, Expert Panel on Musculoskeletal Imaging

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: Catherine C. Roberts, MD; Richard H. Daffner, MD; Barbara N. Weissman, MD; D. Lee Bennett, MD; Judy S. Blebea, MD; Jon A. Jacobson, MD; William B. Morrison, MD; Charles S. Resnik, MD; David A. Rubin, MD; Mark E. Schweitzer, MD; Leanne L. Seeger, MD; Mihra Taljanovic, MD; James N. Wise, MD; William K. Payne, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Manaster BJ, Petersen B, Dalinka MK, Rubin DA, Rosen G, Lackman R, Janjan N, Expert Panel on Musculoskeletal Imaging. Follow-up of malignant or aggressive musculoskeletal tumors. [online publication]. Reston (VA): American College of Radiology (ACR); 2006. 11 p. [46 references]

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [American College of Radiology \(ACR\) Web site](#).

ACR Appropriateness Criteria® *Anytime, Anywhere*™ (PDA application). Available from the [ACR Web site](#).

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- ACR Appropriateness Criteria®. Background and development. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in Portable Document Format (PDF) from the [American College of Radiology \(ACR\) Web site](#).
- ACR Appropriateness Criteria® radiation dose assessment introduction. American College of Radiology. 2 p. Electronic copies: Available from the [American College of Radiology Web site](#).

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on May 6, 2001. The information was verified by the guideline developer as of June 29, 2001. This summary was updated by ECRI on May 22, 2003. The updated information was verified by the guideline developer on June 23, 2003. This NGC summary was updated on August 11, 2006. This summary was updated by ECRI Institute on June 29, 2009.

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